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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/551,304 | 05/18/2006 | Christopher R Trotta | 10589-033-999 | 6447 |

20583 7590 01/16/2008

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| EXAMINER | |
|---|---|
| SHIBUYA, MARK LANCE | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 01/16/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/551,304 | TROTTA, CHRISTOPHER R | |
| | Examiner | Art Unit | |
| | Mark L. Shibuya, Ph.D. | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2,3,6,9-30,33-35,37,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *2, 3, 6, 9-30, 33-35, 37, 39 and 40* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 2, 3, 6, 9-30, 33-35, 37, 39 and 40 are pending.

### *Election of Species*

2. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. This requirement is not for election of Invention.

The species are as follows:

A. Methods comprising a nucleic acid comprising (a) a reporter gene; (b) a substrate labeled with a fluorophore and a quencher; (c) a substrate labeled with a fluorescent donor moiety and a fluorescent acceptor moiety.

B. A method for (a) identifying a compound that modulates fungal tRNA splicing endonuclease or (b) a method of identifying a therapeutic agent for treatment, management, or amelioration of fungal infection or a symptom thereof, (claims 29, 33)

C. Method comprising a particular and specific reporter gene, wherein said gene comprises a tRNA intron.

D. Methods comprising a particular and specific substrate (claims 35).

E. Methods comprising compounds that (a) inhibit activity (claim 12) or (b) enhance activity (claim 13).

F. A particular compound from a combinatorial library, such as peptoid or small organic molecules that are benzodiazepines, (claims 18 19).

G. The method wherein the said compound binds to (a) the fungal tRNA splicing endonuclease, (b) the substrate, or (c) the tRNA intron.

H. Methods comprising determination of (a) cytotoxic activity of the compound or (b) cytostatic activity of the compound.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

**Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141.** If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The claims are deemed to correspond to the species listed above in the following manner:

A. Methods comprising a nucleic acid comprising (a) a reporter gene; (b) a substrate labeled with a fluorophore and a quencher; (c) a substrate labeled with

a fluorescent donor moiety and a fluorescent acceptor moiety. Claims 2, 3, 6, 9, 10, 11, 33.

B. A method for (a) identifying a compound that modulates fungal tRNA splicing endonuclease or (b) a method of identifying a therapeutic agent for treatment, management, or amelioration of fungal infection or a symptom thereof. Claims 29 and 33.

C. Applicant must elect a particular and specific reporter gene, wherein said gene comprises a tRNA intron. Claims 2, 3, and 15.

D. Methods comprising a particular and specific substrate. Claims 6, 9, 10, 11, 33, 35).

E. Methods comprising compounds that (a) inhibit activity (claim 12) or (b) enhance activity (claim 13). Claims 2, 3, 13, 14.

F. A particular compound from a combinatorial library, such as peptoid or small organic molecules that are benzodiazepines. Claims 2, 3, 6, 9, 10, 11, 18 19, 33.

G. The method wherein the said compound (a) binds to the fungal tRNA splicing endonuclease, (b) binds to the substrate, (c) binds to the tRNA intron, (d) disrupts the interaction between the tRNA intron or (e) disrupts an interaction between subunits of the tRNA splicing endonuclease. Claims 24-28

H. Methods comprising determination of (a) cytotoxic activity of the compound or (b) cytostatic activity of the compound. Claims 37 and 39.

The following claim(s) are generic:

Claims 2, 3, 6, 9, 10, 11, 15, 18, 19, 29, 33, 35, 37, 39.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The claims are linked by a technical feature that is a method comprising introducing a member of a library of compounds into an assay for fungal tRNA splicing endonuclease activity and detecting change in the tRNA splicing endonuclease activity. However, it would have been obvious to use such a method in view of the following prior art references.

Rana, WO 01/25486 A1, (IDS filed 7/20/07) discloses assay-derived tRNA inhibiting (e.g., binding: see e.g. bottom of page 9-top of page 10; and claims, especially claims 1, 2, 28-30, 40-43) compounds within the scope of the presently claimed invention (e.g., claims 25-26) that are antifungal for use in treating fungal (e.g. yeast: see claims 47-48) infections (e.g., see page 10-11) when administered to humans. The ability to inhibit tRNA splicing endonuclease is inherently present due to the ability of these compounds to bind RNA (e.g. tRNA). In any event, the claim is not structure-limited and the PTO lacks the facilities for making comparisons between prior art compounds and the claimed prospective assay-derived compounds.

Rana, does not appear to explicitly teach tRNA and tRNA splicing endonuclease activity.

Tocchini-Valentini et al., US 2004/0023239 A1, throughout the publication and e.g., para [0023], [0030], and [0031], teach yeast tRNA splicing endonuclease activity.

Gontarek, WO 00/67580, (IDS filed 7/20/07, cite no. B17), throughout the publication and e.g., at p. 11-13 teach a method comprising introducing a member of a library of compounds into an assay for fungal mRNA splicing activity and detecting change in the mRNA splicing activity.

Wang et al., Nucleic Acids Research Vol. 18, No. 22, pp. 6625-6631, (IDS filed 7/20/07), teach an assay for endonucleolytic tRNA maturation, where inactivated micrococcal nuclease (reversible inhibitor) bound to radiolabeled pre-tRNA physically blocks the sites of endonuclease cleavage and prevents tRNA processing activities present in Fraction III of spinach chloroplasts, presumably by substrate occlusion or "masking", where formation of an inactive micrococcal nuclease enzyme substrate complex precludes utilization of the tRNA substrate by a second enzyme.

LI et al., Science Vol. 280 (4/1999), (IDS filed 7/20/07), teach that the tRNA splicing pathway is analogous in mammals and other organisms (e.g., fungi).

It would have been prima facie obvious at the time the invention was made for one of ordinary skill in the art skill in the art to have combine the method of screening compounds from a library against RNA splicing activity wherein the said activity was fungal tRNA splicing endonuclease activity.

It would have been obvious to use tRNA splicing endonuclease assays in the high throughput screening methods of Rana because Rana specifically suggest screening small molecules libraries for compounds which disrupt tRNA interactions, including splicing, and in light of the secondary reference teaching that tRNA splicing pathway in fungi is known and analogous; and the known teaching of tRNA splicing endonuclease inhibition; with the desirability of using high throughput screening of small molecular libraries for screening enzyme binding compounds as drug candidates. Wang et al. teach inhibition of tRNA processing by blocking endonuclease cleavage in spinach chloroplasts and Li et al. teach tRNA splicing pathway to be analogous in various organism.

One of ordinary skill in the art would have been motivated to use a splicing assays comprising fungal tRNA splicing endonuclease because Tocchini-Valentini et al., US 2004/0023239 A1, throughout the publication and e.g., para [0023], [0030], and [0031], teach yeast tRNA splicing endonuclease activity and because Tocchini-Valentini et al., at para [0002]-[0003] and [0009], teach using tRNA splicing as essential for the formation of functional tRNAs and therefore essential for gene expression.

Therefore the technical feature linking the claims does not represent a contribution over the prior art and so cannot constitute a special technical feature linking the claims. Therefore, unity of invention over the species of the invention is lacking, and the instant requirement for election of species is proper.

3. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya, whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. James Douglas Schultz can be reached on (571) 272-

0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark L. Shibuya, Ph.D.
Primary Examiner
Art Unit 1639